Short-term blood pressure response to mineralocorticoid-receptor blockade in aldosteronisms: Primary hyperaldosteronism versus aldosterone-associated hypertension (low-renin hypertension)

I. Crespo Hernández[1], A. Ortolá Buigues[1], T. Ruiz Gracia[1], E. Gómez Hoyos[2], M. Cuesta Hernández[3], A. Barabash Bustelo[1], MV. Saez De Parayuelo[1], MS. Sanchez-Orta[1], AL. Calle Pascual[1], I. Runkle de la Vega[1]. [1]Hospital Clínico San Carlos, Madrid. [2]Hospital Clínico de Valladolid, Spain. [3]Beaumont Hospital, Dublin, Ireland.

Introduction

Primary aldosteronism is a common cause of secondary hypertension. Some authors consider aldosteronism to be a spectrum, ranging from aldosterone-associated (or low- renin) hypertension (AAH) to primary hyperaldosteronism (PHA) due to bilateral hyperplasia (BAH), with aldosteronoma as a separate entity. Thus, the blood pressure (BP) response to mineralocorticoid-receptor blockade (MRB) could be similar in both AAH and BAH.

Material and methods

We conducted a retrospective analysis of 60 patients with hypertension secondary to aldosteronism. Screening was performed per Endocrine Society Guidelines, considering screening positive with an aldosterone (pg/ml)-to-direct renin (pg/ml) ratio (ARR) ≥ 25.
We used the 25 mg Captopril Test (CAP) as the diagnostic test for PHA, with patients on doxazosine and/or long-acting verapamil treatment. We compared the office BP response to MRB (50-100 mg of spironolactone or 200-300 mg of eplerenone) used as sole BP medication following 2 weeks of therapy in patients with PHA versus AAH. BP: mmHg. Renin and aldosterone were determined by RIA (CIS-BIO). Normal renin : 3-33 pg/ml. Statistical analysis: Mann-Whitney U, Student T, Wilcoxon, and Chi-square Tests. SPSS 15.

Results

Baseline Characteristics of patients with HAP versus AHH: 28/60 versus (vs) 32/60 patients, 67.9% vs 75% women, mean age 55.4 (SD 2.7) vs 53.9 (SD 9.9).
Initial number of blood-pressure-lowering drugs: 2 [IQR 1-2] vs 1 [IQR 1-2]. Resistant hypertension: 6/28 (21.4 %) vs 2/32 (6.3%). Major cardiovascular events and/or renal failure: 8/28 (28.6%) vs 5/32 (15.6%) p=0.06.
Hypokalemia: 5/28 (17.8%) vs 0/32 (0%) p=0.003. Serum Potassium (S K^+) mmol/L: 4.0mmol/L (SD 0.6) vs 4.2 (SD 0.5) (N: 3.5-5.5), Serum Creatinine (S Cr) mg/dl: 1.0 (SD 0.5) vs 0.89 (SD 0.3),

Pre-MRB Office Systolic BP (SBP): 154 (SD 22.6) vs 151 (SD 16.6), Office Diastolic BP (DBP): 90 (SD 14.4) vs 90 (DS 12.1).

RESPONSE TO 2 weeks of MRB:
SBP 128 (SD 15.7) vs 123 (SD 11.8), DBP: 77 (SD 10.7) vs 75(SD 9.1).
S K^+: 4.6(SD:0.5) vs 4.7 (SD 0.5). S Cr: 1.14 (SD 0.7) vs 1.00 (SD 0.4).

The descent in both SBP and DBP was significant in PHA (both p <0.001) as in AAH (both p < 0.001). No significant differences were found in SBP (p = 0.569) nor DBP (p = 0.389) reductions following MRB in PHA vs AAH.

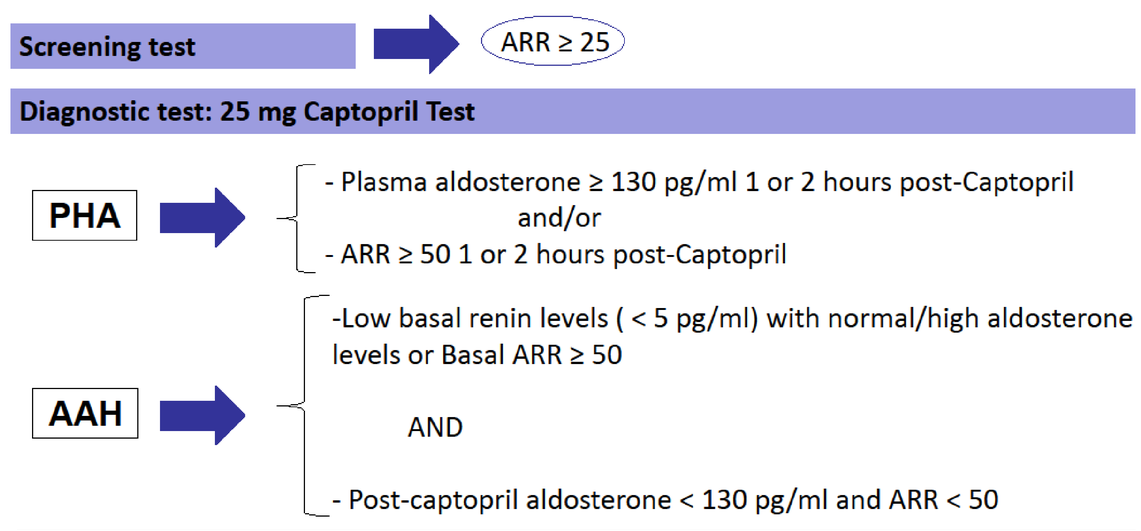

Figure 1. Diagnostic criteria.

	PHA (n=28)	AAH (n=32)
Sex women (%)	67,9	75
Age years , mean (SD)	55,4 (2,7)	53,9 (9,9)
# Antihypertensive drugs Median [IQR]	2 [1-2]	1 [1-2]
S K^+ (mmol/L) Mean (SD)	4 (0.6)	4,2 (0.5)
S Creatinine (mg/dl) Mean (SD)	1 (0.5)	0,89 (0.3)

Figure 2. Basal characteristics. S = Serum.

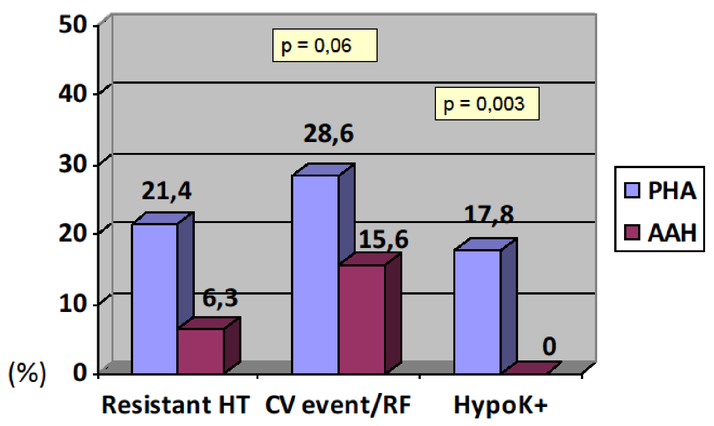

Figure 3. Basal characteristics.
HT: Hypertension. CV: Cardiovascular. RF: Renal failure.

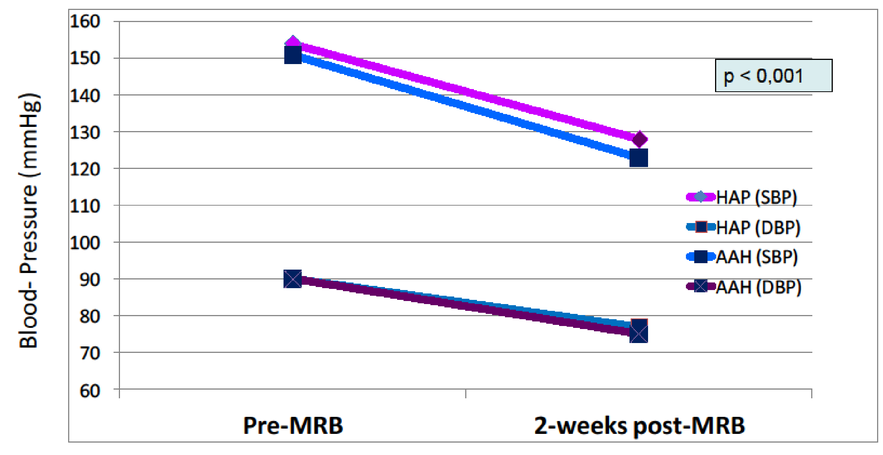

Figure 4. Blood-pressure respond after 2 weeks of treatment.
SBP: Systolic Blood pressure. DBP: Diastolic Blood-pressure.

		Basal	1 hour post-captopril	2 hours post-captopril
Primary Hyperaldosteronism	**Plasma aldosterone** pg/ml	216,5 [165-321]	149 [117-231]	172 [123-217]
	Direct Renin pg/ml	2 [1,2-3]	2 [1-3,2]	2 [1,3-3,2]
	ARR	102,5 [58-167]	75 [57-111]	84,4[58-161]
Aldosterone-related Hypertension	**Plasma aldosterone** pg/ml	139 [105-203]	72 [52-100]	79 [52-92]
	Direct Renin pg/ml	2 [1,3-3,3]	2,5 [1,7-4]	3 [1,5-4]
	ARR	55,3 [44-79]	32,2 [18-42]	30,3 [17-52]

Figure 5. 25 mg Captopril Test results.: median [IQR]

Conclusions

The Captopril Test can identify both patients with Primary Hyperaldosteronism and Aldosterone-related hypertension. Both groups present a similar, dramatic and rapid blood-pressure response to high-dose mineralocorticoid-receptor blockers, suggesting that AAH patients should be identified, and the same protocol for medical therapy used in both PHA and AAH.
Our results support the hypothesis that aldosterone-induced hypertension is a continuum.